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* * * * * Welcome to STN International * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	DEC 21	IPC search and display fields enhanced in CA/CAPLUS with the IPC reform
NEWS	4	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/USPAT2
NEWS	5	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS	6	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS	7	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS	8	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS	9	JAN 30	Saved answer limit increased
NEWS	10	JAN 31	Monthly current-awareness alert (SDI) frequency added to TULSA
NEWS	11	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS	12	FEB 22	Status of current WO (PCT) information on STN
NEWS	13	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS	14	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS	15	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS	16	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS	17	FEB 28	TOXCENTER reloaded with enhancements
NEWS	18	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS	19	MAR 01	INSPEC reloaded and enhanced
NEWS	20	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS	21	MAR 08	X.25 communication option no longer available after June 2006
NEWS	22	MAR 22	EMBASE is now updated on a daily basis
NEWS	23	APR 03	New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS	24	APR 03	Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL
NEWS	25	APR 04	STN AnaVist \$500 visualization usage credit offered
NEWS EXPRESS			FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005. V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT http://download.cas.org/express/v8.0-Discover/
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***** STN Columbus *****

FILE 'HOME' ENTERED AT 10:53:12 ON 06 APR 2006

=> file medline

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'MEDLINE' ENTERED AT 10:53:24 ON 06 APR 2006

FILE LAST UPDATED: 5 APR 2006 (20060405/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).

See also:

<http://www.nlm.nih.gov/mesh/>

http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html

http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s ap2

L1 1149 AP2

=> d ti 1-20

L1 ANSWER 1 OF 1149 MEDLINE on STN

TI Clathrin adaptor **AP2** regulates thrombin receptor constitutive internalization and endothelial cell resensitization.

L1 ANSWER 2 OF 1149 MEDLINE on STN

TI Characterizing medullary and human mesenchymal stem cell-derived adipocytes.

L1 ANSWER 3 OF 1149 MEDLINE on STN

TI Overexpression of suppressor of cytokine signaling 3 in adipose tissue causes local but not systemic insulin resistance.

L1 ANSWER 4 OF 1149 MEDLINE on STN

TI Monkey embryonic stem cells differentiate into adipocytes in vitro.

L1 ANSWER 5 OF 1149 MEDLINE on STN

TI Floral organ identity genes in the orchid *Dendrobium crumenatum*.

L1 ANSWER 6 OF 1149 MEDLINE on STN

TI Isolation of plant transcription factors using a modified yeast one-hybrid system.

L1 ANSWER 7 OF 1149 MEDLINE on STN

TI Delayed radioprotection by nuclear transcription factor kappaB -mediated

induction of manganese superoxide dismutase in human microvascular endothelial cells after exposure to the free radical scavenger WR1065.

- L1 ANSWER 8 OF 1149 MEDLINE on STN
TI Analysis of the interacting partners of the neuronal calcium-binding proteins L-CaBP1, hippocalcin, NCS-1 and neurocalcin delta.
- L1 ANSWER 9 OF 1149 MEDLINE on STN
TI Sorting of Pmel17 to melanosomes through the plasma membrane by AP1 and AP2: evidence for the polarized nature of melanocytes.
- L1 ANSWER 10 OF 1149 MEDLINE on STN
TI APETALA2 regulates the stem cell niche in the Arabidopsis shoot meristem.
- L1 ANSWER 11 OF 1149 MEDLINE on STN
TI Dopamine D3 receptors regulate GABAA receptor function through a phospho-dependent endocytosis mechanism in nucleus accumbens.
- L1 ANSWER 12 OF 1149 MEDLINE on STN
TI Characterization of water extractable organic matter in a deep soil profile.
- L1 ANSWER 13 OF 1149 MEDLINE on STN
TI Conversion of adipogenic to osteogenic phenotype using crystalline porous biomatrices of marine origin.
- L1 ANSWER 14 OF 1149 MEDLINE on STN
TI KLF6 is one transcription factor involved in regulating acid ceramidase gene expression.
- L1 ANSWER 15 OF 1149 MEDLINE on STN
TI Clathrin interaction and subcellular localization of Ce-DAB-1, an adaptor for protein secretion in Caenorhabditis elegans.
- L1 ANSWER 16 OF 1149 MEDLINE on STN
TI Molecular evolution of the AP2 subfamily.
- L1 ANSWER 17 OF 1149 MEDLINE on STN
TI Jasmonate signaling pathway.
- L1 ANSWER 18 OF 1149 MEDLINE on STN
TI The conserved Ala37 in the ERF/AP2 domain is essential for binding with the DRE element and the GCC box.
- L1 ANSWER 19 OF 1149 MEDLINE on STN
TI PPARgamma activity in subcutaneous abdominal fat tissue and fat mass gain during short-term overfeeding.
- L1 ANSWER 20 OF 1149 MEDLINE on STN
TI Cell-specific regulation of TRBP1 promoter by NF-Y transcription factor in lymphocytes and astrocytes.

=> s l1 and diabeetes
0 DIABEETES
L2 0 L1 AND DIABEETES

=> s l1 and diabetes
230216 DIABETES
L3 46 L1 AND DIABETES

=> d ti 1-46

L3 ANSWER 1 OF 46 MEDLINE on STN

TI Ginsenoside 20S-protopanaxatriol (PPT) activates peroxisome proliferator-activated receptor gamma (PPARGgamma) in 3T3-L1 adipocytes.

L3 ANSWER 2 OF 46 MEDLINE on STN
 TI Insulin and oleic acid increase PPARGgamma2 expression in cultured mouse hepatocytes.

L3 ANSWER 3 OF 46 MEDLINE on STN
 TI The role of fatty acid binding proteins in metabolic syndrome and atherosclerosis.

L3 ANSWER 4 OF 46 MEDLINE on STN
 TI Environmental chemical tributyltin augments adipocyte differentiation.

L3 ANSWER 5 OF 46 MEDLINE on STN
 TI Functional characterization of the promoter of the human glucose transporter 10 gene.

L3 ANSWER 6 OF 46 MEDLINE on STN
 TI Adipocyte/macrophage fatty acid binding proteins control integrated metabolic responses in obesity and **diabetes**.

L3 ANSWER 7 OF 46 MEDLINE on STN
 TI Pharmacological profile of a novel, non-TZD PPARGgamma agonist.

L3 ANSWER 8 OF 46 MEDLINE on STN
 TI MCC-555 (Mitsubishi-Tokyo Pharmaceuticals).

L3 ANSWER 9 OF 46 MEDLINE on STN
 TI Adipose tissue model using three-dimensional cultivation of preadipocytes seeded onto fibrous polymer scaffolds.

L3 ANSWER 10 OF 46 MEDLINE on STN
 TI Glucosamine induces lipid accumulation and adipogenic change in C2C12 myoblasts.

L3 ANSWER 11 OF 46 MEDLINE on STN
 TI Thiazolidinediones improve insulin sensitivity in adipose tissue and reduce the hyperlipidaemia without affecting the hyperglycaemia in a transgenic model of type 2 **diabetes**.

L3 ANSWER 12 OF 46 MEDLINE on STN
 TI A high-capacity assay for PPARGgamma ligand regulation of endogenous **ap2** expression in 3T3-L1 cells.

L3 ANSWER 13 OF 46 MEDLINE on STN
 TI Angiotensin type 1 receptor blockers induce peroxisome proliferator-activated receptor-gamma activity.

L3 ANSWER 14 OF 46 MEDLINE on STN
 TI Evidence of impaired adipogenesis in insulin resistance.

L3 ANSWER 15 OF 46 MEDLINE on STN
 TI Benzoxazinones as PPARGgamma agonists. 2. SAR of the amide substituent and in vivo results in a type 2 **diabetes** model.

L3 ANSWER 16 OF 46 MEDLINE on STN
 TI Bone is a target for the antidiabetic compound rosiglitazone.

L3 ANSWER 17 OF 46 MEDLINE on STN
 TI Chronic interleukin-6 (IL-6) treatment increased IL-6 secretion and induced insulin resistance in adipocyte: prevention by rosiglitazone.

L3 ANSWER 18 OF 46 MEDLINE on STN

TI Overexpression of sterol regulatory element-binding protein-1a in mouse adipose tissue produces adipocyte hypertrophy, increased fatty acid secretion, and fatty liver.

L3 ANSWER 19 OF 46 MEDLINE on STN
 TI A novel cellular marker of insulin resistance and early atherosclerosis in humans is related to impaired fat cell differentiation and low adiponectin.

L3 ANSWER 20 OF 46 MEDLINE on STN
 TI Transgenic amplification of glucocorticoid action in adipose tissue causes high blood pressure in mice.

L3 ANSWER 21 OF 46 MEDLINE on STN
 TI Monocyte chemoattractant protein 1 in obesity and insulin resistance.

L3 ANSWER 22 OF 46 MEDLINE on STN
 TI Role of the fatty acid binding protein mab1 in obesity and insulin resistance.

L3 ANSWER 23 OF 46 MEDLINE on STN
 TI The adipocyte lipid binding protein (ALBP/aP2) gene facilitates foam cell formation in human THP-1 macrophages.

L3 ANSWER 24 OF 46 MEDLINE on STN
 TI Transplantation of adipose tissue lacking leptin is unable to reverse the metabolic abnormalities associated with lipodystrophy.

L3 ANSWER 25 OF 46 MEDLINE on STN
 TI Expression of resistin in the adipose tissue is modulated by various factors including peroxisome proliferator-activated receptor alpha.

L3 ANSWER 26 OF 46 MEDLINE on STN
 TI The chlorophyll-derived metabolite phytanic acid induces white adipocyte differentiation.

L3 ANSWER 27 OF 46 MEDLINE on STN
 TI An aminophospholipid translocase associated with body fat and type 2 diabetes phenotypes.

L3 ANSWER 28 OF 46 MEDLINE on STN
 TI Upregulation of bone morphogenetic protein GDF-3/Vgr-2 expression in adipose tissue of FABP4/aP2 null mice.

L3 ANSWER 29 OF 46 MEDLINE on STN
 TI Agouti regulates adipocyte transcription factors.

L3 ANSWER 30 OF 46 MEDLINE on STN
 TI A-ZIP/F-1 mice lacking white fat: a model for understanding lipodystrophic diabetes.

L3 ANSWER 31 OF 46 MEDLINE on STN
 TI Up-regulation of peroxisome proliferator-activated receptors (PPAR-alpha) and PPAR-gamma messenger ribonucleic acid expression in the liver in murine obesity: troglitazone induces expression of PPAR-gamma-responsive adipose tissue-specific genes in the liver of obese diabetic mice.

L3 ANSWER 32 OF 46 MEDLINE on STN
 TI Regulation of leptin by agouti.

L3 ANSWER 33 OF 46 MEDLINE on STN
 TI Fenofibrate and rosiglitazone lower serum triglycerides with opposing effects on body weight.

L3 ANSWER 34 OF 46 MEDLINE on STN
 TI Increased levels of nuclear SREBP-1c associated with fatty livers in two mouse models of **diabetes** mellitus.

L3 ANSWER 35 OF 46 MEDLINE on STN
 TI Altered insulin secretion associated with reduced lipolytic efficiency in **aP2**^{-/-} mice.

L3 ANSWER 36 OF 46 MEDLINE on STN
 TI Leptin reverses insulin resistance and **diabetes** mellitus in mice with congenital lipodystrophy.

L3 ANSWER 37 OF 46 MEDLINE on STN
 TI A novel method for analysis of nuclear receptor function at natural promoters: peroxisome proliferator-activated receptor gamma agonist actions on **aP2** gene expression detected using branched DNA messenger RNA quantitation.

L3 ANSWER 38 OF 46 MEDLINE on STN
 TI Insulin resistance and **diabetes** mellitus in transgenic mice expressing nuclear SREBP-1c in adipose tissue: model for congenital generalized lipodystrophy.

L3 ANSWER 39 OF 46 MEDLINE on STN
 TI Life without white fat: a transgenic mouse.

L3 ANSWER 40 OF 46 MEDLINE on STN
 TI Dietary conjugated linoleic acid normalizes impaired glucose tolerance in the Zucker diabetic fatty fa/fa rat.

L3 ANSWER 41 OF 46 MEDLINE on STN
 TI Troglitazone action is independent of adipose tissue.

L3 ANSWER 42 OF 46 MEDLINE on STN
 TI Uncoupling of obesity from insulin resistance through a targeted mutation in **aP2**, the adipocyte fatty acid binding protein.

L3 ANSWER 43 OF 46 MEDLINE on STN
 TI Expression of the adipocyte fatty acid-binding protein in streptozotocin-**diabetes**: effects of insulin deficiency and supplementation.

L3 ANSWER 44 OF 46 MEDLINE on STN
 TI Antidiabetic agent pioglitazone enhances adipocyte differentiation of 3T3-F442A cells.

L3 ANSWER 45 OF 46 MEDLINE on STN
 TI Targeted expression of a toxin gene to adipose tissue: transgenic mice resistant to obesity.

L3 ANSWER 46 OF 46 MEDLINE on STN
 TI Fatty acid regulation of gene expression. Transcriptional and post-transcriptional mechanisms.

=> file ca

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

1.17

1.38

FILE 'CA' ENTERED AT 10:55:23 ON 06 APR 2006

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FILE COVERS 1907 - 30 Mar 2006 VOL 144 ISS 15
FILE LAST UPDATED: 30 Mar 2006 (20060330/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3

1967 AP2
104009 DIABETES
L4 84 L1 AND DIABETES

=> d ti 1-10

L4 ANSWER 1 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Lipid-amino acid conjugates and methods of use

L4 ANSWER 2 OF 84 CA COPYRIGHT 2006 ACS on STN
TI BLX-1002 lowers blood glucose in non obese diabetic (NOD) and streptozotocin (STZ) induced diabetic mice with strong effect in TNF and IL-6

L4 ANSWER 3 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Insulin and oleic acid increase PPAR γ 2 expression in cultured mouse hepatocytes

L4 ANSWER 4 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Pharmacological profile of a novel, non-TZD PPAR γ agonist

L4 ANSWER 5 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Environmental chemical tributyltin augments adipocyte differentiation

L4 ANSWER 6 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Functional characterization of the promoter of the human glucose transporter 10 gene

L4 ANSWER 7 OF 84 CA COPYRIGHT 2006 ACS on STN
TI The role of fatty acid binding proteins in metabolic syndrome and atherosclerosis

L4 ANSWER 8 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Preparation of azolylamino benzobicyclooctanecarboxamides as modulators of activator protein-1 (AP-1) and/or NF- κ B activity.

L4 ANSWER 9 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Fused aryl and heteroaryl bicyclo[2.2.2]octane derivative modulators of the glucocorticoid receptor, AP-1, and/or NF- κ B activity, and therapeutic use thereof

L4 ANSWER 10 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Sulfonylurea Agents Exhibit Peroxisome Proliferator-activated Receptor

γ Agonistic Activity

=> d ti 11-20

- L4 ANSWER 11 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Analysis of gene expression profiles in insulin-sensitive tissues from pre-diabetic and diabetic Zucker diabetic fatty rats
- L4 ANSWER 12 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Corepressors selectively control the transcriptional activity of PPAR γ in adipocytes
- L4 ANSWER 13 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Thiazolidinediones improve insulin sensitivity in adipose tissue and reduce the hyperlipidaemia without affecting the hyperglycaemia in a transgenic model of type 2 **diabetes**
- L4 ANSWER 14 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Preparation of amino acid derivatives as methionine aminopeptidase-2 inhibitors
- L4 ANSWER 15 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Characteristics of circadian gene expressions in mice white adipose tissue and 3T3-L1 adipocytes
- L4 ANSWER 16 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Adipocyte/macrophage fatty acid binding proteins control integrated metabolic responses in obesity and **diabetes**
- L4 ANSWER 17 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Specific labeling of mouse 3T3-L1 preadipocyte cell line with green fluorescent protein
- L4 ANSWER 18 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Glucosamine induces lipid accumulation and adipogenic change in C2C12 myoblasts
- L4 ANSWER 19 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Angiotensin Type 1 Receptor Blockers Induce Peroxisome Proliferator-Activated Receptor- γ Activity
- L4 ANSWER 20 OF 84 CA COPYRIGHT 2006 ACS on STN
TI A high-capacity assay for PPAR γ ligand regulation of endogenous aP2 expression in 3T3-L1 cells

=> d 13 ab

- L4 ANSWER 13 OF 84 CA COPYRIGHT 2006 ACS on STN
AB Aim/hypothesis: The aim of this study was to examine the effects of thiazolidinediones on the MKR mouse model of type 2 **diabetes**.
Methods: Six-week-old wild-type (WT) and MKR mice were fed with or without rosiglitazone or pioglitazone for 3 wk. Blood was collected from the tail vein for serum biochem. anal. Hyperinsulinemic-euglycemic clamp anal. was performed to study effects of thiazolidinediones on insulin sensitivity of tissues in MKR mice. Northern blot anal. was performed to measure levels of target genes of PPAR γ agonists in white adipose tissue and hepatic gluconeogenic genes. Results: Thiazolidinedione treatment of MKR mice significantly lowered serum lipid levels and increased serum adiponectin levels but did not affect levels of blood glucose and serum insulin. Hyperinsulinemic-euglycemic clamp showed that whole-body insulin sensitivity and glucose homeostasis failed to improve in MKR mice after rosiglitazone treatment. Insulin suppression of hepatic endogenous

glucose production failed to improve in MKR mice following rosiglitazone treatment. This lack of change in hepatic insulin insensitivity was associated with no change in the ratio of HMW : total adiponectin, hepatic triglyceride content, and sustained hepatic expression of PPAR γ and stearoyl-CoA desaturase 1 mRNA. Interestingly, rosiglitazone markedly enhanced glucose uptake by white adipose tissue with a parallel increase in CD36, aP2 and GLUT4 gene expression.

Conclusions/interpretation: These data suggest that potentiation of insulin action on tissues other than adipose tissue is required to mediate the antidiabetic effects of thiazolidinediones in our MKR diabetic mice.

=> d 13

L4 ANSWER 13 OF 84 CA COPYRIGHT 2006 ACS on STN
AN 142:385597 CA
TI Thiazolidinediones improve insulin sensitivity in adipose tissue and reduce the hyperlipidaemia without affecting the hyperglycaemia in a transgenic model of type 2 **diabetes**
AU Kim, H.; Haluzik, M.; Gavrilova, O.; Yakar, S.; Portas, J.; Sun, H.; Pajvani, U. B.; Scherer, P. E.; LeRoith, D.
CS Molecular and Cellular Physiology Section, Diabetes Branch, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), Bethesda, MD, 20892-1758, USA
SO Diabetologia (2004), 47(12), 2215-2225
CODEN: DBTGAI; ISSN: 0012-186X
PB Springer GmbH
DT Journal
LA English
RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ti 21-30

L4 ANSWER 21 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Cannabinoid analogs as peroxisome proliferator activated nuclear receptorgamma activators

L4 ANSWER 22 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Preparation of substituted tetralins and indanes as PPAR α modulators for treatment of syndrome X

L4 ANSWER 23 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Identification of Telmisartan as a Unique Angiotensin II Receptor Antagonist With Selective PPAR γ -Modulating Activity

L4 ANSWER 24 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Evidence of impaired adipogenesis in insulin resistance

L4 ANSWER 25 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Site and mechanism of leptin action in a rodent form of congenital lipodystrophy

L4 ANSWER 26 OF 84 CA COPYRIGHT 2006 ACS on STN
TI STAT 5A promotes adipogenesis in non-precursor cells

L4 ANSWER 27 OF 84 CA COPYRIGHT 2006 ACS on STN
TI cDNA and protein sequences of human adipocyte factors regulation protein and their use in drug screening and therapeutics

L4 ANSWER 28 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Bone is a target for the antidiabetic compound rosiglitazone

L4 ANSWER 29 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Benzoxazinones as PPAR γ Agonists. 2. SAR of the Amide Substituent
and In Vivo Results in a Type 2 **Diabetes** Model

L4 ANSWER 30 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Effects of a PPAR γ Agonist, GI262570, on Renal Filtration Fraction
and Nitric Oxide Level in Conscious Rats

=> d 29

L4 ANSWER 29 OF 84 CA COPYRIGHT 2006 ACS on STN
AN 140:146074 CA
TI Benzoxazinones as PPAR γ Agonists. 2. SAR of the Amide Substituent
and In Vivo Results in a Type 2 **Diabetes** Model
AU Rybczynski, Philip J.; Zeck, Roxanne E.; Dudash, Joseph, Jr.; Combs,
Donald W.; Burris, Thomas P.; Yang, Maria; Osborne, Melville C.; Chen,
Xiaoli; Demarest, Keith T.
CS Johnson and Johnson Pharmaceutical Research and Development L.L.C.,
Raritan, NJ, 08869, USA
SO Journal of Medicinal Chemistry (2004), 47(1), 196-209
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 140:146074
RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ab 29

L4 ANSWER 29 OF 84 CA COPYRIGHT 2006 ACS on STN
AB A series of benzoxazinones I [R = Me, n-decyl, 2-cyclopentylethyl,
HOCH₂CH₂, H₂NCO(CH₂)₄, MeCF₂(CH₂)₄, EtO(CH₂)₃, etc.] has been synthesized
and tested for PPAR γ agonist activity (PPAR = peroxisome
proliferator-activated receptor). Synthetic approaches were developed to
provide either racemic or chiral compds. In vitro functional potency
could be measured through induction of the **ap2** gene, a target of
PPAR γ . These studies revealed that compds. I with large aliphatic
chains at the nitrogen of the benzoxazinone ring are the most potent.
Substitution of the chain was tolerated and in many cases enhanced the in
vitro potency of the compound. Select compds. were further tested for
metabolic stability, oral bioavailability in rats, and efficacy in db/db
mice after 11 days of dosing. In vivo anal. with optically active (R)-I
[R = n-hexyl, MeO(CH₂)₄] demonstrated that the series has potential for
the treatment of type 2 **diabetes**.

=> d ti 31-40

L4 ANSWER 31 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Chronic interleukin-6 (IL-6) treatment increased IL-6 secretion and
induced insulin resistance in adipocyte: prevention by rosiglitazone

L4 ANSWER 32 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Ragaglitazar: A novel PPAR α & PPAR γ agonist with potent
lipid-lowering and insulin-sensitizing efficacy in animal models

L4 ANSWER 33 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Gene expression regulation of adipocytes response to modulated insulin
signaling and diagnostic uses for metabolic disorders

L4 ANSWER 34 OF 84 CA COPYRIGHT 2006 ACS on STN

TI Benzoxazinones as PPAR γ agonists. Part 1: SAR of three aromatic regions

L4 ANSWER 35 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Overexpression of Sterol regulatory element-binding protein-1 α in mouse adipose tissue produces adipocyte hypertrophy, increased fatty acid secretion, and fatty liver

L4 ANSWER 36 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI A novel cellular marker of insulin resistance and early atherosclerosis in humans is related to impaired fat cell differentiation and low adiponectin

L4 ANSWER 37 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Effect of leptin on fatless mice

L4 ANSWER 38 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Transgenic amplification of glucocorticoid action in adipose tissue causes high blood pressure in mice

L4 ANSWER 39 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Monocyte chemoattractant protein 1 in obesity and insulin resistance

L4 ANSWER 40 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Inhibition of adipogenesis and development of glucose intolerance by soluble preadipocyte factor-1 (pref-1)

=> d ti 41-50

L4 ANSWER 41 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Preparation of benzoic acid and benzenealkanoic acid dual inhibitors of adipocyte fatty acid binding protein and keratinocyte fatty acid binding protein

L4 ANSWER 42 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Biologically active 4H-benzo[1,4]oxazin-3-ones useful as PPAR γ agonists or antagonists

L4 ANSWER 43 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI The chlorophyll-derived metabolite phytanic acid induces white adipocyte differentiation

L4 ANSWER 44 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Role of the fatty acid binding protein mal-1 in obesity and insulin resistance

L4 ANSWER 45 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI The adipocyte lipid binding protein (ALBP/aP2) gene facilitates foam cell formation in human THP-1 macrophages

L4 ANSWER 46 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Preparation of pyrazinone inhibitors of fatty acid binding protein for treatment of **diabetes** and related diseases

L4 ANSWER 47 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI An aminophospholipid translocase associated with body fat and type 2 **diabetes** phenotypes

L4 ANSWER 48 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Expression of resistin in the adipose tissue is modulated by various factors including peroxisome proliferator-activated receptor α

L4 ANSWER 49 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Transplantation of adipose tissue lacking leptin is unable to reverse the

metabolic abnormalities associated with lipoatrophy

L4 ANSWER 50 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Preparation of pyridone derivatives as **aP2** inhibitors for
treatment of Type II **diabetes**

=> d 46

L4 ANSWER 46 OF 84 CA COPYRIGHT 2006 ACS on STN
AN 138:122657 CA
TI Preparation of pyrazinone inhibitors of fatty acid binding protein for
treatment of **diabetes** and related diseases
IN Sulsky, Richard; Robl, Jeffrey A.
PA Bristol-Myers Squibb Company, USA
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003006023	A1	20030123	WO 2002-US22186	20020712
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003040516	A1	20030227	US 2002-194028	20020712
	US 6919323	B2	20050719		
	EP 1414461	A1	20040506	EP 2002-749992	20020712
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
PRAI	US 2001-305356P	P	20010713		
	WO 2002-US22186	W	20020712		

OS MARPAT 138:122657

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ab 46

L4 ANSWER 46 OF 84 CA COPYRIGHT 2006 ACS on STN
AB The title compds. I [R = (un)substituted alkyl, etc.; A = bond, methylene, etc.; X = CONHOH, etc.; Z = (un)substituted aryl], useful as inhibitors of fatty acid binding protein (no data), are prepared A method is also provided for treating **diabetes** and related diseases, especially Type II **diabetes**, employing such **aP2** inhibitors alone or in combination with other therapeutic agents, including other antidiabetic agent such as metformin, glyburide, troglitazone and/or insulin.

=> d 50

L4 ANSWER 50 OF 84 CA COPYRIGHT 2006 ACS on STN
AN 136:386024 CA
TI Preparation of pyridone derivatives as **aP2** inhibitors for
treatment of Type II **diabetes**

IN Sulsky, Richard; Robl, Jeffrey A.
 PA Bristol-Myers Squibb Company, USA
 SO PCT Int. Appl., 55 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002040448	A1	20020523	WO 2001-US43647	20011120
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2436854	AA	20020523	CA 2001-2436854	20011120
	AU 2002037664	A5	20020527	AU 2002-37664	20011120
	US 2002077340	A1	20020620	US 2001-989212	20011120
	US 6670380	B2	20031230		
	EP 1343763	A1	20030917	EP 2001-986468	20011120
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004536023	T2	20041202	JP 2002-542776	20011120
PRAI	US 2000-252014P	P	20001120		
	WO 2001-US43647	W	20011120		
OS	MARPAT 136:386024				

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ab 50

L4 ANSWER 50 OF 84 CA COPYRIGHT 2006 ACS on STN
 AB Title compds. I [wherein A = R1, (CR3R4)nR1, (CR3R4)mR5(CR6R7)pR1, or (CR3R4)n(CR6R7)pR1; Q = R2, (CR3R4)nR2, R5(CR3R4)pR2, (CR11R12)mR5(CR6R7)pR2, (CR11R12)n(CR6R7)pR2, SOR2, or SO2R2; R1 and R2 = independently H or (un)substituted (cyclo)alkyl, (cyclo)alkenyl, (hetero)aryl, (hetero)araryl, hetero(cyclo)aralkyl, or cycloheteroalkyl; R3 and R4 = independently, H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, alkoxy-carbonyl, alkyl-carbonyl, (alkyl)aminocarbonyl, arylaminocarbonyl, aryl-carbonyl, (hetero)aryl, halo, OH, alkoxy, or aryloxy; or CR3R4 = ring; R5 = a bond, O, NR8, S, SO, "SO2, CO, or CONH; R6 and R7 = independently H, (cyclo) alkyl, aryl, OH, NH2, halo, alkoxy, aryloxy, alkylthio, arylthio, (di)alkylamino, (di)arylamino, alkoxy-carbonyl, alkylaminocarbonyl, or alkylcarbonylamino; R8 = H, aryl(carbonyl), alkylaminocarbonyl, arylaminocarbonyl, alkoxy-carbonyl, aryloxy-carbonyl, or alkyl(carbonyl); R9 and R10 = independently H, (cyclo)alkyl, (hetero)aryl, or aralkyl; R11 and R12 = independently H or (un)substituted (cyclo)alkyl, (cyclo)alkenyl, (hetero)aryl, (hetero)aralkyl, or cycloheteroalkyl; X = Z, (CR3R4)nZ, CH:CHZ, or cycloalkyl-Z; Z = CO2R9, CONHOH, CONR9R10, (CR3R4)mOH, tetrazolyl; n = 0-5; m = 1-5; p = 0-4; with provisos] were prepared as adipocyte fatty binding protein (aP2) inhibitors. For example, Et 5-carboxy-2-pyridone was treated with N-iodosuccinimide in MeOH to give 1,6-dihydro-5-iodo-6-oxo-3-pyridinecarboxylic acid Et ester (86%). N-alkylation with 2,4-dichlorophenylmethyl iodide (98%), followed by arylation with 4-bromophenylboronic acid in the presence of PPh3, TEA, and Pd(OAc)2 (52%), afforded 5-(4-bromophenyl)-1-[(2,4-dichlorophenyl)methyl]-1,6-dihydro-6-oxo-3-pyridinecarboxylic acid Et ester. Deesterification (99%), reduction using borane dimethylsulfide complex (52%), bromination (99%), conversion to the nitrile using KCN in DMF

(48%), and oxidation to the pyridineacetic acid (89%) produced II. I are useful for the prevention and treatment of **diabetes** and related diseases, especially Type II **diabetes**, and may be employed in combination with another antidiabetic agent such as metformin, glyburide, troglitazone and/or insulin (no data).

=> d ti 51-60

- L4 ANSWER 51 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Downregulated IRS-1 and PPAR γ in obese women with gestational **diabetes**: relationship to FFA during pregnancy
- L4 ANSWER 52 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Protein and cDNA sequence a of a novel human transcription factor AP-2 sequence homolog and therapeutical uses
- L4 ANSWER 53 OF 84 CA COPYRIGHT 2006 ACS on STN
TI MCC-555 (Mitsubishi-Tokyo Pharmaceuticals)
- L4 ANSWER 54 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Preparation of lactam inhibitors of factor Xa which are useful for the treatment of thrombosis
- L4 ANSWER 55 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Method for activating peroxisome proliferator activated receptor- γ -controlled genes
- L4 ANSWER 56 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Upregulation of bone morphogenetic protein GDF-3/Vgr-2 expression in adipose tissue of FABP4/**aP2** null mice
- L4 ANSWER 57 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Biologically active 4H-benzo[1,4]oxazin-3-ones useful as PPAR γ agonists or antagonists
- L4 ANSWER 58 OF 84 CA COPYRIGHT 2006 ACS on STN
TI FOXC2 is a winged helix gene that counteracts obesity, hypertriglyceridemia, and diet-induced insulin resistance
- L4 ANSWER 59 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Preparation of tetrahydropyrimidone inhibitors of fatty acid binding protein
- L4 ANSWER 60 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Agouti regulates adipocyte transcription factors

=> d ti 61-84

- L4 ANSWER 61 OF 84 CA COPYRIGHT 2006 ACS on STN
TI A-ZIP/F-1 mice lacking white fat: a model for understanding lipotrophic **diabetes**
- L4 ANSWER 62 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Up-regulation of peroxisome proliferator-activated receptors (PPAR- α) and PPAR- γ messenger ribonucleic acid expression in the liver in murine obesity: troglitazone induces expression of PPAR- γ -responsive adipose tissue-specific genes in the liver of obese diabetic mice
- L4 ANSWER 63 OF 84 CA COPYRIGHT 2006 ACS on STN
TI Heterocyclylbiphenyl **aP2** inhibitors

L4 ANSWER 64 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Methods of screening protease inhibitors, of inducing mice susceptible to HIV protease inhibitor-induced dyslipidemia, and genes associated therewith

L4 ANSWER 65 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Fenofibrate and Rosiglitazone Lower Serum Triglycerides with Opposing Effects on Body Weight

L4 ANSWER 66 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Leptin is a potent anti-diabetic in mice with lipodystrophy and insulin resistance

L4 ANSWER 67 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Method for treating atherosclerosis employing an **ap2** inhibitor, and pharmaceutical combinations with other agents

L4 ANSWER 68 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Method for treating **diabetes** employing an **ap2** inhibitor and combination

L4 ANSWER 69 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Increased levels of nuclear SREBP-1c associated with fatty livers in two mouse models of **diabetes** mellitus

L4 ANSWER 70 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Altered insulin secretion associated with reduced lipolytic efficiency in **ap2**^{-/-} mice

L4 ANSWER 71 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Leptin reverses insulin resistance and **diabetes** mellitus in mice with congenital lipodystrophy

L4 ANSWER 72 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Insulin resistance and **diabetes** mellitus in transgenic mice expressing nuclear SREBP-1c in adipose tissue: model for congenital generalized lipodystrophy

L4 ANSWER 73 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Life without white fat: a transgenic mouse

L4 ANSWER 74 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI The short- and long-term effects of tumor necrosis factor- α and BRL 49653 on peroxisome proliferator-activated receptor (PPAR) γ 2 gene expression and other adipocyte genes

L4 ANSWER 75 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Dietary conjugated linoleic acid normalizes impaired glucose tolerance in the Zucker diabetic fatty fa/fa rat

L4 ANSWER 76 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Troglitazone action is independent of adipose tissue

L4 ANSWER 77 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI The thiazolidinedione insulin sensitizer, BRL 49653, increases the expression of PPAR- γ and **ap2** in adipose tissue of high-fat-fed rats

L4 ANSWER 78 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI D-Glucose-induced dysmorphogenesis of embryonic kidney

L4 ANSWER 79 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Uncoupling of obesity from insulin resistance through a targeted mutation in **ap2**, the adipocyte fatty acid binding protein

L4 ANSWER 80 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Genes of energy balance: modulation in transgenic mice

L4 ANSWER 81 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Transgenic GLUT-4 overexpression in fat enhances glucose metabolism: preferential effect on fatty acid synthesis

L4 ANSWER 82 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Expression of the adipocyte fatty acid-binding protein in streptozotocin-diabetes: effects of insulin deficiency and supplementation

L4 ANSWER 83 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Targeted expression of a toxin gene to adipose tissue: transgenic mice resistant to obesity

L4 ANSWER 84 OF 84 CA COPYRIGHT 2006 ACS on STN
 TI Antidiabetic agent pioglitazone enhances adipocyte differentiation of 3T3-F442A cells

=> d 63,68,84

L4 ANSWER 63 OF 84 CA COPYRIGHT 2006 ACS on STN
 AN 133:296436 CA
 TI Heterocyclylbiphenyl **ap2** inhibitors
 IN Robl, Jeffrey A.; Sulsky, Richard B.; Magnin, David R.
 PA Bristol-Myers Squibb Co., USA
 SO PCT Int. Appl., 206 pp.
 CODEN: PIXXD2

DT Patent
 LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000059506	A1	20001012	WO 2000-US7417	20000320
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6548529	B1	20030415	US 2000-519079	20000306
	CA 2366871	AA	20001012	CA 2000-2366871	20000320
	BR 2000009563	A	20020115	BR 2000-9563	20000320
	EP 1181014	A1	20020227	EP 2000-918177	20000320
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	TR 200102874	T2	20020321	TR 2001-200102874	20000320
	JP 2002541106	T2	20021203	JP 2000-609070	20000320
	EE 200100504	A	20021216	EE 2001-504	20000320
	NZ 513493	A	20040227	NZ 2000-513493	20000320
	ZA 2001006856	A	20021120	ZA 2001-6856	20010820
	LT 4921	B	20020625	LT 2001-92	20010925
	BG 105968	A	20020531	BG 2001-105968	20011002
	NO 2001004823	A	20011004	NO 2001-4823	20011004
	LV 12782	B	20020620	LV 2001-155	20011102
	US 2003199563	A1	20031023	US 2002-321137	20021217
	US 6927227	B2	20050809		
PRAI	US 1999-127745P	P	19990405		
	US 2000-519079	A3	20000306		

WO 2000-US7417 W 20000320
 OS MARPAT 133:296436
 RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 68 OF 84 CA COPYRIGHT 2006 ACS on STN
 AN 132:231969 CA
 TI Method for treating **diabetes** employing an **aP2**
 inhibitor and combination
 IN Robl, Jeffrey A.; Parker, Rex A.; Biller, Scott A.; Jamil, Haris;
 Jacobson, Bruce L.; Kodukula, Krishna
 PA Bristol-Myers Squibb Co., USA
 SO PCT Int. Appl., 55 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000015229	A1	20000323	WO 1999-US20946	19990913
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2344309	AA	20000323	CA 1999-2344309	19990913
	AU 9963877	A1	20000403	AU 1999-63877	19990913
	AU 754488	B2	20021114		
	BR 9913833	A	20010529	BR 1999-13833	19990913
	TR 200100773	T2	20010723	TR 2001-200100773	19990913
	EP 1121129	A1	20010808	EP 1999-951438	19990913
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	TR 200100774	T2	20011221	TR 2001-200100774	19990913
	EE 200100154	A	20021216	EE 2001-154	19990913
	EE 4356	B1	20041015		
	NZ 510209	A	20030725	NZ 1999-510209	19990913
	NO 2001001351	A	20010511	NO 2001-1351	20010316
	LT 4871	B	20011227	LT 2001-22	20010316
	LT 4870	B	20011227	LT 2001-23	20010316
	BG 105431	A	20011231	BG 2001-105431	20010410
	LV 12686	B	20011020	LV 2001-57	20010412
	US 2002035064	A1	20020321	US 2001-905235	20010713
	ZA 2002007430	A	20030916	ZA 2002-7430	20020916
	ZA 2002007433	A	20031027	ZA 2002-7433	20020916
	US 2004229807	A1	20041118	US 2004-872721	20040621
PRAI	US 1998-100677P	P	19980917		
	US 1999-390275	B1	19990907		
	WO 1999-US20946	W	19990913		
	US 2001-905235	B1	20010713		

OS MARPAT 132:231969
 RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 84 OF 84 CA COPYRIGHT 2006 ACS on STN
 AN 119:173989 CA
 TI Antidiabetic agent pioglitazone enhances adipocyte differentiation of 3T3-F442A cells
 AU Sandouk, Tagrid; Reda, Domenic; Hofmann, Cecilia
 CS Stritch Sch. Med., Loyola Univ., Maywood, IL, 60153, USA

SO American Journal of Physiology (1993), 264(6, Pt. 1), C1600-C1608
CODEN: AJPHAP; ISSN: 0002-9513
DT Journal
LA English

=> d ab 63, 68, 84

L4 ANSWER 63 OF 84 CA COPYRIGHT 2006 ACS on STN

AB **AP2** inhibiting biphenyls substituted in the 2-position by a substituted 5-membered heterocycle and in the 3'-position by a carboxyalkyl, carboxyalkenyl, carboxymethoxy, carboxymethylamino, or 5-tetrazolylmethyl group, were prepared. The compds. are useful for treating **diabetes** and related diseases, especially Type II **diabetes** (no data) and may be used in combination with another antidiabetic agent such as metformin, glyburide, troglitazone and/or insulin. Thus, 2-BrC6H4CO2H was treated with benzoin and the resulting keto ester cyclized to give 2-(2-bromophenyl)-4,5-diphenyloxazole which was coupled with 3-OHC6H4B(OH)2 to give the biphenyl derivative I [R = CHO]. Reduction of the formyl group, chlorination, and reaction with NaCN gave I [R = CH2CN] which was cyclized with Me3SnN3 to give I [R = 5-tetrazolylmethyl].

L4 ANSWER 68 OF 84 CA COPYRIGHT 2006 ACS on STN

AB A method is provided for treating **diabetes** and related diseases, such as insulin resistance, obesity, hyperglycemia, hyperinsulinemia, elevated blood levels of free fatty acids or glycerol, hypertriglyceridemia, and especially Type II **diabetes**, employing an adipocyte protein **ap2** inhibitor or a combination of an **ap2** inhibitor and another antidiabetic agent such as metformin, glyburide, troglitazone and/or insulin.

L4 ANSWER 84 OF 84 CA COPYRIGHT 2006 ACS on STN

AB Adipocytes play an important role in normal physiol. as a major site for systemic energy homeostasis. In disorders such as **diabetes**, adipocyte function is markedly altered. In this study, the authors investigated the effect of pioglitazone, a novel antidiabetic agent known to lower plasma glucose in animal models of **diabetes** mellitus, on cellular differentiation and expression of adipose-specific genes. Treatment of confluent 3T3-F442A preadipocyte cultures for 7 days with pioglitazone (Pio; 1 µM) and insulin (Ins; 0.17 µM) resulted in >95% cell differentiation into lipid-accumulating adipocytes in comparison with 60-80% cell differentiation by treatment with either agent alone. Anal. of triglyceride accumulation showed increases of triglyceride content over time above untreated preadipocytes by treatment of the cells with Ins, Pio, and especially with Ins + Pio. Basal glucose transport, as measured by cellular uptake of 2-deoxy-D-[14C]glucose, was likewise enhanced in a time-dependent manner by treatment of preadipocytes with Ins, Pio, or Ins + Pio, such that a synergistic effect resulted from the combined treatment with both agents. It was further determined that RNA transcript abundance for genes encoding glucose transporters GLUT-1 and GLUT-4, as well as the adipose-specific genes encoding adipsin and **ap2**, were increased by the Ins, Pio, or Ins + Pio treatment. Taken together, these findings indicate that pioglitazone is a potent adipogenic agent. By promoting differentiation, this agent may move cells into a state active for glucose uptake, storage, and metabolism.

=> file reg

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TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

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SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

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* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
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experimental property data in the original document. For information
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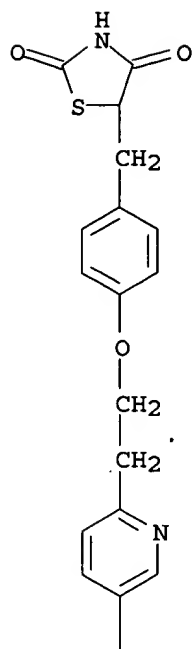
=> s pioglitazone
L5 5 PIOGLITAZONE

=> d 1

L5 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN
RN 414355-31-0 REGISTRY
ED Entered STN: 12 May 2002
CN 2,4-Thiazolidinedione, 5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]-
, mononitrate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Pioglitazone nitrate
MF C19 H20 N2 O3 S . H N O3
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

CM 1

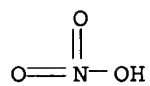
CRN 111025-46-8
CMF C19 H20 N2 O3 S



CM 2

CRN 7697-37-2

CMF H N O3



- 1 REFERENCES IN FILE CA (1907 TO DATE)
- 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
- 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)